Claims

1. An immunogenic composition comprising an IL-13 element that is capable of driving an immune response that recognises human IL-13 and one or more foreign T-cell epitopes.

2. An immunogenic composition as claimed in claim 1, wherein the T-cell epitopes are foreign with respect to both human self-proteins and with respect to IL-13 sequences from other species.

3. An immunogenic composition as claimed in claim 1 or claim 2, wherein the T-cell helper epitopes are short peptide sequences added to the IL-13 sequence or are comprised within a carrier protein.

4. An immunogenic composition as claimed in claim 3 wherein the carrier protein is selected from *Haemophilus influenzae* Protein D and CPC (clyta-P2-clyta).

5. An immunogenic composition as claimed in claim 3 or 4, wherein the carrier protein and IL-13 element form a fusion protein.

6. An immunogenic composition as claimed in claim 3, wherein short T-cell epitopes are added to the IL-13 sequence by an addition or substitution event within, or at the terminal ends, of the IL-13 sequence by synthetic, recombinant or molecular biological means.

7. An immunogenic composition as claimed in claim 6 wherein the short T-cell epitope is a promiscuous epitope.

8. An immunogenic composition as claimed in claim 7 wherein the promiscuous epitope is selected from P2 and P30 from tetanus toxoid.

9. An immunogenic composition as claimed in claim 1, wherein the IL-13 element comprises the entire human IL-13 sequence, or functional equivalent fragments thereof.

10. An immunogenic composition as claimed in claim 9 wherein the IL-13 element is in mutated form.

11. An immunogenic composition as claimed in claim 10, wherein the mutated IL-13 is in the form of a chimaeric IL-13 formed by substituting amino acids with amino acids that are found in equivalent positions within an IL-13 sequence from another mammalian species.

12. An immunogenic composition as claimed in claim 11, wherein the substitutions occur in areas that are associated with alpha helical regions.

13. An immunogenic composition as claimed in claim 11 or 12 wherein the substitutions involve amino acids taken from more than one different non-human mammalian species.

14. An immunogenic composition as claimed in claim 1 wherein the IL-13 element are human chimaeric IL-13 sequences which have a similar conformational shape to native human IL-13 whilst having sufficient amino acid sequence diversity to enhance its immunogenicity when administered to a human, characterised in that the chimaeric IL-13 immunogen has the sequence of human IL-13 comprising:

(a) substitution mutations in at least two of the following alpha helical regions: PSTALRELIEELVNIT, MYCAALESLI, KTQRMLSGF or AQFVKDLLLHLKKLFRE,

(b) comprises in unmutated form at least six of the following regions of high inter-species conservation 3PVP, 12ELIEEL, 19NITQ, 28LCN, 32SMVWS, 50SL, 60AI, 64TQ, 87DTKIEVA, 99LL, 106LF, and

(c) optionally comprises a mutation in any of the remaining amino acids,

wherein any substitution performed in steps a, b or c is a structurally conservative substitution.

15. An immunogenic composition as claimed in claim 14, wherein greater than 50% of these substitutions or mutations comprise amino acids taken from equivalent positions within the IL-13 sequence of a non-human.

16. An immunogenic composition as claimed in claim 14 or 15, wherein greater than 50% of these substitutions or mutations occur in regions of human IL-13 which are predicted to be alpha helical in configuration.

17. An immunogenic composition as claimed in claim 14, 15 or 16, wherein the immunogen comprises between 2 and 20 substitutions.

18. An immunogenic composition as claimed in claim 1 wherein the IL-13 element is based on an non-human IL-13 sequence wherein the non-human surface exposed regions are substituted for the equivalent human sequences.

19. An immunogenic composition as claimed in claim 14, wherein the amino acid sequence of human IL-13 comprises conservative substitutions, or substitutions characteristic of amino acids present at equivalent positions within the IL-13 sequence of a non-human species, present in at least six of the following 13 positions 8T, 11R, 18V, 49E, 62K, 66M, 69G, 84H, 97K, 101L, 105K, 109E, 111R.

20. An immunogenic composition as claimed in claim 19 comprising at least 6 of the following substitutions:

Position	Substitution
8	T->S
11	R->K
18	V->A
49	E->D
62	K->R
66	M->I
69	G->A
84	H->R
97	K->T
101	L->V
105	K->R
109	E->Q
111	R->T

21. An immunogenic composition as claimed in claim 1, wherein the IL-13 element is selected from the following group: Immunogen 1, Immunogen 11, Immunogen 12 and Immunogen 13.

22. An immunogenic composition as claimed in claim 1, selected from the following group: Immunogen 2, Immunogen 3, Immunogen 7, Immunogen 8, Immunogen 9 and Immunogen 10.

23. An immunogenic composition as claimed in any one of claims 1 to 22 further comprising a mutation in the human IL-13 element that abolishes the biological activity of the immunogen and is selected from the following group: E 12 to I, S, or Y; E12 to K; R 65 to D; S 68 to D; R 108 to D.

24. A method of designing an immunogenic composition as claimed in claim 1 comprising:

(a) taking the sequence of human IL-13 and identifying regions that are predicted to form an alpha helical structure, and

(b) mutating the sequence of human IL-13 within these alpha helical regions to substitute amino acids from the human sequence with amino acids that are either a conservative substitution or are found in equivalent positions within the IL-13 sequence of a different species, and

c) attaching or inserting a source of T-cell epitopes that are foreign with respect to any human self epitope and also foreign with respect to any mammalian IL-13 sequence.

25. A method for the manufacture of a human chimaeric IL-13 immunogen which has a similar conformational shape to native human IL-13 whilst having sufficient amino acid sequence diversity to enhance its immunogenicity when administered to a human, the method comprising the following steps:

(a) taking the sequence of human IL-13 and performing at least one substitution mutation in at least two of the following alpha helical regions: PSTALRELIEELVNIT, MYCAALESLI, KTQRMLSGF or AQFVKDLLLHLKKLFRE,

(b) preserving at least six of the following regions of high inter-species conservation 3PVP, 12ELIEEL, 19NITQ, 28LCN, 32SMVWS, 50SL, 60AI, 64TQ, 87DTKIEVA, 99LL, 106LF,

(c) optionally mutating any of the remaining amino acids, and

(d) attaching a source of T-cell epitopes that are foreign with respect to any human self epitope and also foreign with respect to any mammalian IL-13 sequence,

characterised in that any substitution performed in steps a, b or c is a structurally conservative substitution.

26. A method for the manufacture of a human chimaeric IL-13 immunogen as claimed in claim 25, wherein all four alpha helical regions comprise at least one substitution mutation.

27. A method for the manufacture of a human chimaeric IL-13 immunogen as claimed in claim 25, wherein all 11 of the regions are unmutated.

28. A method for the manufacture of a human chimaeric IL-13 immunogen which has a similar conformational shape to native human IL-13 whilst having sufficient amino acid sequence diversity to enhance its immunogenicity when administered to a human, the method comprising the following steps:

(a) aligning IL-13 amino acid sequences from different species,

(b) identifying regions of high variability and high conservation,

(c) taking the sequence of human IL-13 and mutating it in the areas of high variability to substitute amino acids from the human sequence with amino acids that are either a conservative substitution or are found in equivalent positions within the IL-13 sequence of a different species, and

(d) attaching a source of T-cell epitopes that are foreign with respect to any human self epitope and also foreign with respect to any mammalian IL-13 sequence,

29. A method for the manufacture of a human chimaeric IL-13 immunogen as claimed in any one of claims 24 to 28, wherein all greater than 50% of these substitutions or mutations comprise amino acids taken from equivalent positions within the IL-13 sequence of a non-human species.

30. A method for the manufacture of a human chimaeric IL-13 immunogen as claimed in any one of claims 24 to 28, wherein greater than 50% of these substitutions or mutations occur in regions of human IL-13 which are predicted to be alpha helical in configuration.

31. A method for the manufacture of a human chimaeric IL-13 immunogen as claimed in any one of claims 24 to 28, wherein substitutions or mutations comprise amino acids taken from equivalent positions within at least two non-human IL-13 sequences.

32. A method for the manufacture of a human chimaeric IL-13 immunogen as claimed in any one of claims 24 to 28, wherein the immunogen comprises between 6 and 20 substitutions, and most preferably between 6 and 10 substitutions.

33. An immunogen that is derivable from any of the methods claimed in claims 24 to 28, wherein the immunogens are immunogenic, when formulated in an appropriate manner for a vaccine, in a human vaccinee.

34, A vaccine comprising an immunogen as claimed in any one of claims 1 to 23 or claim 33.

35. A polynucleotide vaccine comprising a polynucleotide that encodes an immunogen as claimed in claimed in any one of claims 1 to 23 or claim 33.

36. A method of treating an individual suffering from or being susceptible to COPD, asthma or atopic dermatitis, comprising administering to that individual a vaccine as claimed in claim 34, and thereby raising in that individual a serum neutralising anti-IL-13 immune

response and thereby ameliorating or abrogating the symptoms of COPD, asthma or atopic dermatitis.

37. A method of treatment of asthma as claimed in claim 36 comprising one or more of the following clinical effects:

- A reduction in airway hyper-responsiveness (AHR)
- A reduction in mucus hyper-secretion and goblet cell metaplasia
- A reduction in sub-epithelial fibrosis of the airways
- 4. A reduction in eosinophil levels
- 5. A reduction in the requirement for the use of inhaled corticosteroids (ICS) would also be a feature of successful treatment using an IL13 autovaccine.

38. A method of treatment of atopic dermatitis as claimed in claim 36, comprising one or more of the following clinical effects:

- A reduction in skin irritation
- A reduction in itching and scratching
- A reduction in the requirement for conventional treatment.
- if applicable a reduction in the requirement for the use of topical corticosteroids. An ideal IL13 autovaccine could potentially make ICS steroid treatment redundant, although a reduction in the 'frequency of use' or 'dose required' of ICS is also envisaged as a valuable outcome.